

In re Application of:  
Rheins et al.

Application No.: 09/375,689

Filed: August, 17, 1999

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Attorney Docket No.: DERM1100-1

**EXHIBIT B: CLAIMS AS THEY WILL STAND UPON ENTRY OF THE AMENDMENT**

64. (Amended) A non-invasive method for obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample, the method comprising:

(a) applying at least one application of an adhesive to the skin and removing the adhesive from the skin in a manner such that the skin nucleic acid profile prior to application and after application is not affected and such that a sample comprising a nucleic acid adheres to the adhesive after its removal, or, scraping the skin with an instrument to remove a sample comprising a nucleic acid from the skin, thereby obtaining a skin sample comprising a nucleic acid; and

(b) isolating or detecting the nucleic acid from the skin sample of step (a).

65. The method of claim 64, wherein the skin sample consists essentially of stratum corneum.

66. The method of claim 64, wherein the skin sample consists essentially of stratum lucidum cells.

67. The method of claim 64, wherein the skin sample consists essentially of stratum granulosum cells.

68. The method of claim 64, wherein the skin sample consists essentially of stratum spinosum cells.

69. The method of claim 64, wherein the skin sample consists essentially of stratum basalis cells.

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70. The method of claim 64, wherein an adhesive surface is applied one time to the skin.
71. The method of claim 70, wherein an adhesive surface is applied two or more times to the skin.
72. The method of claim 65, wherein the stratum corneum skin sample is isolated by one application of an adhesive surface to an outer layer of the skin.
73. The method of claim 64, wherein the adhesive surface comprises an adhesive tape.
74. The method of claim 73, wherein the adhesive tape comprises a duct tape, a Scotch™ tape or a D-SQUAME™ tape.
75. The method of claim 64, wherein a skin sample is isolated by scraping an outer layer of skin with a rigid instrument.
76. The method of claim 64, wherein the nucleic acid comprises a DNA.
77. The method of claim 64, wherein the nucleic acid comprises an RNA.
78. The method of claim 77, wherein the RNA comprises an mRNA.
79. The method of claim 78, wherein the nucleic acid encodes a polypeptide.
80. The method of claim 79, wherein the polypeptide comprises a cytokine.
81. The method of claim 79, wherein the polypeptide comprises an interleukin.

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82. (Amended) The method of claim 79, wherein the cytokine comprises interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-3 (IL-3), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-6 (IL-6), interleukin-7 (IL-7), interleukin-8 (IL-8), interleukin-9 (IL-9), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13), interleukin-14 (IL-14), granulocyte macrophage colony stimulating factor (GM-CSF), or an interferon, or any combination thereof.

83. The method of claim 78, wherein the polypeptide comprises an inflammatory mediator.

84. The method of claim 83, wherein the inflammatory mediator comprises a leukotriene or a prostaglandin.

85. The method of claim 64, further comprising identifying or quantifying the nucleic acid.

86. The method of claim 85, wherein identifying or quantifying the nucleic acid is by a polymerase chain reaction (PCR).

87. The method of claim 85, wherein identifying or quantifying the nucleic acid is by hybridization with a polynucleotide probe.

88. The method of claim 85, wherein identifying or quantifying the nucleic acid is by RNase protection assay.

89. The method of claim 85, wherein by identifying or quantifying a nucleic acid in a recovered sample the presence of a local or systemic disease, a disorder, a genetic disease, or an inflammatory reaction is identified, distinguished, or diagnosed.

90. The method of claim 64, wherein the nucleic acid is associated with a local biological reaction.

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91. The method of claim 64, wherein the nucleic acid is associated with a systemic biological reaction.
92. The method of claim 64, further comprising applying the sample to a chip.
93. The method of claim 64, wherein the skin sample is a human skin sample.
94. The method of claim 64, further comprising applying the cellular material sample to a chip.
95. A non-invasive method for isolating a nucleic acid in a skin cell of a subject comprising:
- a) removing an outer skin layer to expose an inner skin layer by scraping or stripping by use of an adhesive;
  - (b) removing an inner skin sample from the exposed skin by scraping or stripping by use of an adhesive; and,
  - (c) isolating or detecting a nucleic acid sample from the inner skin sample.
96. The method of claim 95, wherein the outer skin layer comprises a stratum corneum.
97. (Amended) The method of claim 95, wherein the adhesive comprises an adhesive tape.
98. The method of claim 95, wherein the nucleic acid comprises a DNA.
99. The method of claim 95, wherein the nucleic acid comprises an RNA.
100. The method of claim 99, wherein the nucleic acid encodes a polypeptide.
101. The method of claim 95, further comprising identifying or quantifying the nucleic acid.

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102. The method of claim 95, further comprising applying the nucleic acid, or complementary equivalent, to a chip.

103. The method of claim 95, wherein the skin sample is a human skin sample.

104. (Amended) A non-invasive method for obtaining a skin sample for use in isolating or detecting nucleic acid encoding a cytokine in the skin sample, the method comprising:

applying at least one application of an adhesive surface to the skin and removing the adhesive surface from the skin such that a skin sample comprising nucleic acid in an amount sufficient for subsequent isolation or detection adheres to the adhesive surface after its removal and in a manner such that the skin nucleic acid profile prior to application and after application is not affected, thereby obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample.

105. The method of claim 104, wherein the skin sample consists essentially of stratum corneum.

106. The method of claim 105, wherein the stratum corneum is isolated by one application of an adhesive surface to an outer layer of the skin.

107. The method of claim 104, wherein the skin sample consists essentially of stratum lucidum cells.

108. The method of claim 104, wherein the skin sample consists essentially of stratum granulosum cells.

109. The method of claim 104, wherein the skin sample consists essentially of stratum spinosum cells.

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110. The method of claim 104, wherein the skin sample consists essentially of stratum basalis cells.
111. The method of claim 104, wherein the at least one application is one application.
112. The method of claim 104, wherein the at least one application is two or more applications.
113. The method of claim 104, wherein the adhesive surface comprises an adhesive tape.
114. The method of claim 113, wherein the adhesive tape comprises a duct tape, a Scotch™ tape or a D-SQUAME™ tape.
115. The method of claim 104, wherein the skin sample is isolated by scraping an outer layer of skin with a rigid instrument.
116. The method of claim 104, wherein the nucleic acid is DNA.
117. The method of claim 104, wherein the nucleic acid is RNA.
118. The method of claim 117, wherein the RNA is mRNA.
119. The method of claim 104, wherein the nucleic acid is a combination of DNA and RNA.
120. (Amended) The method of claim 104, wherein the nucleic acid encodes a polypeptide.
121. The method of claim 120, wherein the polypeptide is a cytokine.
122. The method of claim 120, wherein the polypeptide is an interleukin.

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123. (Amended) The method of claim 121, wherein the cytokine is interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-3 (IL-3), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-6 (IL-6), interleukin-7 (IL-7), interleukin-8 (IL-8), interleukin-9 (IL-9), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13), interleukin-14 (IL-14), granulocyte macrophage colony stimulating factor (GM-CSF), or an interferon or any combination thereof.

124. (Amended) The method of claim 121, wherein the cytokine is an inflammatory mediator.

125. The method of claim 124, wherein the inflammatory mediator is a leukotriene or a prostaglandin.

126. The method of claim 104, wherein the nucleic acid is present in a local biological reaction.

127. The method of claim 104, wherein the nucleic acid is present in a systemic biological reaction.

128. The method of claim 104, further comprising applying the sample to a chip.

129. The method of claim 104, wherein the skin sample is a human skin sample.

130. The method of claim 104, further comprising isolating or detecting one or more nucleic acids in the skin sample.

131. The method of claim 130, wherein the one or more nucleic acids are amplified by a polymerase chain reaction (PCR) following or during isolation.

132. The method of claim 130, wherein isolating or detecting one or more nucleic acids is by hybridization with a polynucleotide probe.

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133. The method of claim 130, wherein isolating or detecting one or more nucleic acids is by RNase protection assay.

134. The method of claim 130, further comprising applying the nucleic acid to a chip.

135. A non-invasive method for obtaining a skin sample for use in isolating or detecting nucleic acid in the skin sample, the method comprising:

scraping the skin with an instrument to remove a skin sample comprising nucleic acid in an amount sufficient for subsequent isolation or detection, thereby obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample.

136. A non-invasive method for obtaining a skin sample for use in isolating or detecting a nucleic acid in a skin sample, the method comprising:

- (a) scraping the skin with an instrument to remove a sample comprising a nucleic acid from the skin, thereby obtaining a skin sample comprising a nucleic acid;
- (b) isolating or detecting the nucleic acid from the skin sample of step (a).